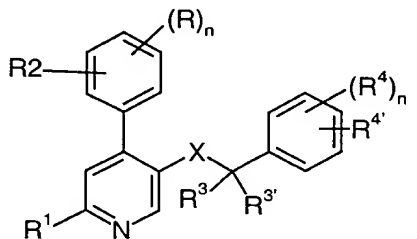


Claims:

1. A compound of the formula



wherein

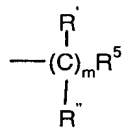
R is hydrogen or halogen;

R¹ is $-(C\equiv C)_mR^{1'}$ or $-(CR'=CR'')_mR^{1'}$

wherein R^{1'} is

a) hydrogen or halogen,

b) cyano, or the following groups:



c) ,

d) $-C(O)NR'R''$,

e) $-C(O)O(CH_2)_mR^5$,

f) $-C(O)R^5$,

g) $-N(OH)-(CH_2)_mR^5$,

h) $-NR'C(O)-(CH_2)_mR^5$,

i) $-N[C(O)-R']_2$,

j) $-OR^6$,

k) $-(CH_2)_m-SR^6$, $-(CH_2)_m-S(O)R^6$, or $-(CH_2)_m-S(O)_2R^6$,

l) aryl, unsubstituted or substituted by one or more substituents, selected from halogen,

trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$,

m) is a five or six membered aromatic heterocycle, containing one to four heteroatoms,

selected from N, O or S and, unsubstituted or substituted by one or more

Sub
~~AB~~

[illegible]

R^4/R^4' are hydrogen, halogen, CF_3 , lower alkyl or lower alkoxy;

R and R^2 or R^4 and R^4' may be together $-CH=CH-CH=CH-$, unsubstituted or substituted by one or two substituents selected from lower alkyl, halogen or lower alkoxy;

X is $-C(O)N(R^8)-$, $(CH_2)_pO-$, $-(CH_2)_pN(R^8)-$, $-N(R^8)C(O)-$ or $-N(R^8)-(CH_2)_p-$; wherein R^8 is hydrogen or lower alkyl;

n is 1 or 2;

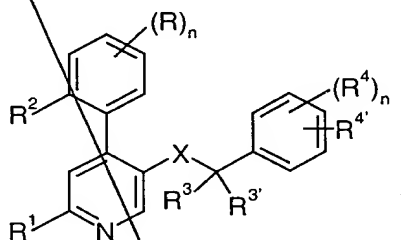
m is 0, 1, 2, 3 or 4;

o is 1 or 2; and

p is 1 or 2;

or a pharmaceutically acceptable acid addition salt thereof.

2. A compound of the formula



wherein

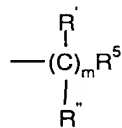
R is hydrogen or halogen;

R^1 is $-(C\equiv C)_mR^{1'}$ or $-(CR'=CR'')_mR^{1'}$

wherein $R^{1'}$ is

a) halogen,

b) cyano, or the following groups:



c)

d) $-C(O)NR'R''$,

e) $-C(O)O(CH_2)_mR^5$,

f) $-C(O)R^5$,

g) $-N(OH)-(CH_2)_mR^5$,

h) $-NR'C(O)-(CH_2)_mR^5$,

i) $-N[C(O)-R']_2$,

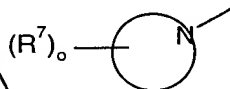
j) $-OR^6$,

k) $-SR^6$, $-S(O)R^6$, or $-S(O)_2R^6$,

l) aryl, unsubstituted or substituted by at least one substituent, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$,

m) is a five or six membered heteroaryl group, containing one to four heteroatoms, selected from N, O or S and is unsubstituted or substituted by at least one substituent, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)OR'$, $-C(O)NR'R''$ or $-C(O)R'$,

n) is a five or six membered non-aromatic heterocycle of the formula



or a five or six membered non-aromatic heterocycle containing one additional heteroatom, selected from N, O or S,

R'/R'' are hydrogen, lower alkyl, cycloalkyl or aryl,

unsubstituted or substituted by at least one substituent, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'''R''''$, nitro, $-(CH_2)_nOR'''$, $-C(O)NR'''R''''$, $-C(O)OR'''$ or $-C(O)R'''$,

R'''/R'''' are independently from each other hydrogen, lower alkyl, cycloalkyl or aryl,

R^5 is hydrogen, cyano, hydroxy, halogen, trifluoromethyl, $-C(O)OR'$ or aryl, unsubstituted or substituted by at least one substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$, or is a five or six membered

heteroaryl group, containing one to four heteroatoms, selected from N, O or S and is unsubstituted or substituted by at least one substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$,

R^6 is hydrogen, lower alkyl, trifluoromethyl, or aryl,

unsubstituted or substituted by at least one substituents, selected from halogen,

Sub A1
-N[C(O)-cycloalkyl]₂, -N(R)C(O)-(CH₂)_mOH, pyridin-2,3,4-yl or phenyl, unsubstituted or substituted by lower alkyl, lower alkoxy or hydroxy or is morpholinyl or piperazinyl, substituted by -C(O)-(CH₂)_mOH or oxy group(s),

R is hydrogen or lower alkyl;

R² is lower alkyl or halogen;

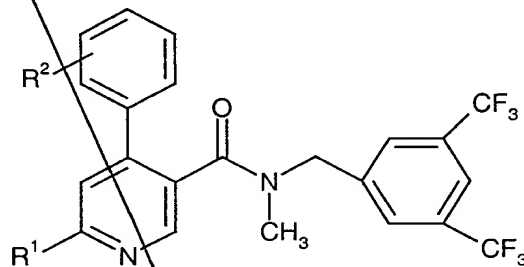
R³/R^{3'} are hydrogen or lower alkyl;

X is -C(O)N(R⁸)- or -N(R⁸)C(O)-;

R⁸ is hydrogen or lower alkyl; and

m is 1 or 2.

4. A compound according to claim 1 having the formula



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wherein R¹ and R² are as defined above.

5. A compound according to claim 4, further comprising R² being lower alkyl.

6. A compound according to claim 5 further comprising R² being 2-methyl.

7. A compound according to claim 6 further comprising R¹ being an unsubstituted or substituted five or six membered non-aromatic heterocycle containing at least one nitrogen or one nitrogen and one additional hetero atom selected from the group N, O or S.

8. A compound according to claim 7 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-hydroxyacetyl-piperazin-1-yl)-N-methyl-4-o-tolyl-nicotinamide.

- Sch
A1
9. A compound according to claim 7 wherein the compound is 4-o-tolyl-1',2',3',6'-tetrahydro-[2,4']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide.
10. A compound according to claim 6 further comprising R¹ being aryl substituted by at least one substituent.
11. A compound according to claim 10 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-methoxy-phenyl)-N-methyl-4-o-tolyl-nicotinamide.
12. A compound according to claim 10 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-hydroxymethyl-phenyl)-N-methyl-4-o-tolyl-nicotinamide.
13. A compound according to claim 6 further comprising R¹ being a five or six member hetero aryl group containing one to four heteroatoms substituted by at least one substituent.
14. A compound according to claim 13 wherein the compound is 2'-methyl-4-o-tolyl-[2,4']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide.
15. A compound according to claim 13 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(3-methyl-[1,2,4]oxadiazol-5-yl)-4-o-tolyl-nicotinamide
16. A compound according to claim 6 further comprising R¹ being unsubstituted hetero aryl.
17. A compound according to claim 16 wherein the compound is 4-o-tolyl-[2,4']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide.
18. A compound according to claim 16 wherein the compound is 4-o-tolyl-[2,3']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide.
19. A compound according to claim 6 further comprising R¹ being cyano.
20. A compound according to claim 19 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-cyanomethyl-N-methyl-4-o-tolyl-nicotinamide.
21. A compound according to claim 6 further comprising R¹ being -(CH₂)_m-S(O)R⁶.

22. A compound according to claim 21 wherein the compound is (RS)-N-(3,5-bis-trifluoromethyl-benzyl)-6-(2-hydroxy-ethanesulfinylmethyl)-N-methyl-4-o-tolyl-nicotinamide.

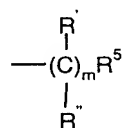
23. A compound according to claim 21 wherein the compound is (RS)-N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(pyridine-2-sulfinyl)-4-o-tolyl-nicotinamide.

24. A compound according to claim 6 further comprising R^1 being $-OR^6$.

25. A compound according to claim 24 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-hydroxymethyl-N-methyl-4-o-tolyl-nicotinamide.

26. A compound according to claim 24 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-(3-hydroxy-propoxy)-N-methyl-4-o-tolyl-nicotinamide.

27. A compound according to claim 6 further comprising R^1 being



wherein R' , R'' , R^5 and m are as above.

28. A compound according to claim 27 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-(3-cyano-propyl)-N-methyl-4-o-tolyl-nicotinamide.

29. A compound according to claim 6 further comprising R^1 being $-(CH_2)_m-SR^6$, and m is as above.

30. A compound according to claim 29 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(1-methyl-1H-imidazol-2-ylsulfanylmethyl)-4-o-tolyl-nicotinamide.

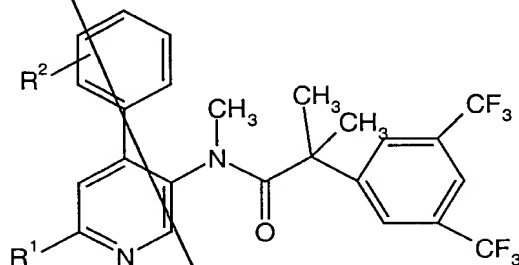
31. A compound according to claim 6 further comprising R^1 being $-(CH_2)_m-S(O)_2R^6$, with m and R^6 as above.

32. A compound according to claim 31 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(pyridine-2-sulfonyl)-4-o-tolyl-nicotinamide.

33. A compound according to claim 4 further comprising R^1 and R^2 being halogen.

34. A compound according to claim 33 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-chloro-4-(4-fluoro-phenyl)-N-methyl-nicotinamide.

35. A compound according to claim 1 having the structure



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wherein R^1 and R^2 are as above.

36. A compound according to claim 35 further comprising R^1 being halogen.

37. A compound according to claim 36 wherein said halogen is chlorine.

38. A compound according to claim 37 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-chloro-4-o-tolyl-pyridin-3-yl)-N-methyl-isobutyramide.

39. A compound according to claim 35 further comprising R^2 being halogen.

40. A compound according to claim 39 wherein said halogen is 2-chloro.

41. A compound according to claim 40 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-6-[hydroxy-(2-hydroxy-ethyl)-amino]-pyridin-3-yl]-N-methyl-isobutyramide.
42. A compound according to claim 40 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-6-(3-oxo-morpholin-4-yl)-pyridin-3-yl]-N-methyl-isobutyramide.
43. A compound according to claim 40 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-2'-methyl-[2,4']bipyridinyl-5-yl]-N-methyl-isobutyramide.
44. A compound according to claim 35 further comprising R^2 being lower alkyl.
45. A compound according to claim 44 wherein R^2 is methyl.
46. A compound according to claim 45 wherein R^1 is $-NR'C(O)-(CH_2)_mR^5$ and R' , R^5 and m are as above.
47. A compound according to claim 46 wherein the compound is acetic acid (5-[[2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl]-methyl-amino]-4-o-tolyl-pyridin-2-ylcarbamoyl)-methyl ester.
48. A compound according to claim 46 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(2-hydroxy-acetyl-amino)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.
49. A compound according to claim 46 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(hydroxyacetyl-methyl-amino)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.
50. A compound according to claim 45 further comprising R^1 being a five or six membered non-aromatic heterocycle of the formula



or a five or six membered non-aromatic heterocycle containing one additional heteroatom, selected from N, O or S and wherein R^7 and o are as above.

51. A compound according to claim 50 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(2,5-dioxo-pyrrolidin-1-yl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.

52. A compound according to claim 50 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(3-oxo-morpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-isobutyramide.

53. A compound according to claim 45 further comprising R^1 being $-N[C(O)-R']_2$ and wherein R' is as above.

54. A compound according to claim 53 wherein the compound is cyclopropanecarboxylic acid (5-{[2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl]-methyl-amino}-4-o-tolyl-pyridin-2-yl)-cyclopropanecarbonyl-amide.

55. A compound according to claim 45 further comprising R^1 being $-N(OH)-(CH_2)_mR^5$, wherein R' , m and R^5 are as above.

56. A compound according to claim 55 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-{6-[hydroxy-(2-hydroxy-ethyl)-amino]-4-o-tolyl-pyridin-3-yl}-N-methyl-isobutyramide.

57. A compound according to claim 45 further comprising R^1 being $-(C\equiv C)_mR^{1'}$ and wherein m and $R^{1'}$ are as above.

58. A compound according to claim 57 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-ethynyl-4-o-tolyl-pyridin-3-yl)-N-methyl-isobutyramide.

59. A compound according to claim 57 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-hydroxy-prop-1-ynyl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.
60. A compound according to claim 45 further comprising R^1 being $-C(O)O(CH_2)_mR^5$ and wherein m and R^5 are as above.
61. A compound according to claim 60 wherein the compound is 5-{{2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl]-methyl-amino}-4-o-tolyl-pyridine-2-carboxylic acid methyl ester.
62. A compound according to claim 45 further comprising R^1 being $-OR^6$ and wherein R^6 is as defined above.
63. A compound according to claim 62 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-hydroxy-4-o-tolyl-pyridin-3-yl)-N-methyl-isobutyramide.
64. A compound according to claim 45 further comprising R^1 being $-(CH_2)_m-S(O)R^6$ and wherein m and R^6 are as defined above.
65. A compound according to claim 64 wherein the compound is (RS)-2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-methoxy-benzenesulfinyl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.
66. A compound according to claim 45 further comprising R^1 being a five or six membered aromatic heterocycle, containing one to four heteroatoms, selected from N, O or S and, unsubstituted or substituted by one or more substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)OR'$, $-C(O)NR'R''$ or $-C(O)R'$, and wherein n, R' and R'' are as above.

67. A compound according to claim 67 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-hydroxymethyl-isoxazol-5-yl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.

68. A method of alleviating the symptoms of patient having a disease state treatable by modulation of NK-1 receptor antagonists comprising administering an effective amount of a medicament containing a sufficient quantity of the compound of claim 1.

69. A medicament containing a compound of claim 1 and at least one pharmaceutically acceptable excipient

70. A medicament according to ~~claim~~ 69 for the treatment of diseases related to NK-1 receptor antagonists.

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